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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/719,646		Francesca Chiodi	0380-P02373U	3240

110 7590 02/11/2004

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/719,646	CHIODI, FRANCESCA	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-52* is/are pending in the application.

4a) Of the above claim(s) *41-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group XVI (claims 49-52, SEQ ID NO: 4) in the Paper received October 31, 2003 is acknowledged. The traversal is on the ground(s) that Groups I-VIII and Groups XIII-XX satisfy the requirements of unity of invention under the PCT and that the claims of Groups XIII-XXX be considered one group. The Examiner has reviewed the arguments and they are found partially persuasive. The methods of Groups XIII-XX will be examined as one entire group The remainder of the requirement set forth April 1, 2003 is still deemed proper and is therefore made FINAL.

2. Claims 41-52 are pending.

Claims 41-48, drawn to non-elected claims are not examined on the merits.

Claims 49-52 are examined on the merits.

Claim Objections

3. Claim 50 is objected to because of the following informality: it references a non-elected claim, claim 46. For purposes of examination the Examiner interprets claim 50 to be dependent from claim 49. Correction is required.

Sequence Compliance

4. This application contains sequence disclosures on page 4, lines 1-8; page 5, lines 15 and 20; and page 43, lines 7-9 that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). This application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicants are requested to review the entire specification and amend it to include the sequence identifiers ensuring that these added SEQ ID numbers are not new matter.

Claim Rejections - 35 USC § 112

Claim Rejections - 35 U.S.C. § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 52 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 52 broadly reads on the administration to a subject an antibody molecule ore a mixture of antibody molecules with at least one additional component. The data presented in the specification is based on *in vitro* studies and the recitation "...administration of the composition to a human" reads on *in vivo* experimentation. Applicants have not presented an animal model whereby the affects of the composition to be administered are evaluated. One skilled in the art cannot reasonable conclude that the results yielded from an *in vitro* study could be extrapolated to an *in vivo* therapy. And while it is not compulsory upon Applicants to present date with absolute predictability with respect to the practice of every possible embodiment of a claimed invention the claims must be enabled.

The claim is directed to and *in vivo* treatment and such a treatment, in and of itself, is unpredictable because pharmacokinetic factors such as the stability of molecules (i.e. antibody, antigen binding fragment) in the body, half-life, absorption efficiency, binding affinity for target cells, biotransformation, and the rate of clearance from the body are important consideration for the efficacy, and thus the practical utility, of the claimed subject matter and yet have not been considered. In the absence of these considerations, there is no assurance (i.e. it is unpredictable) that the active molecules would be available in an effective dose at the target sites and for periods of time sufficient to affect the required cellular or biological responses. *In vitro* models and/or animal models cannot be correlated by one skilled in the art to humans because of the unpredictability of the discussed pharmacokinetic factors.

Additionally, when the intended use for a compound is to be in humans, then the data provided must either be clinical data or can be an animal model or in vitro data, if these models can readily be correlated to utility in humans. Applicants have not provided any correlatable data. Applicants have not shown that the use of the claimed method in any animals is a practical utility nor have Applicants correlated the use of any animal model to humans. The state of the art does not recognize that the claimed method utilizing the compounds listed in the claims or analogous compounds can readily be used *in vivo.* Likewise, those of skill in the art know it that discovery or disclosure of a cascade of biological responses and their effects is not sufficient to support an effective treatment regimen. Skilled artisans recognize that the field of in vivo therapy is both complex and unpredictable, requiring extensive experimentation, producing few treatments, which are actually effective to produce a desired result. Further, those of skill in the art recognize that *in vitro* assays are generally useful to screen the effects of agents on target cells. However, clinical correlations are generally lacking. The greatly increased complexity of the *in vivo* experiment as compared to the very narrowly defined and controlled conditions of an *in vitro* assay does not permit a single extrapolation of *in vitro* assays to mammal or human therapy with any reasonable degree of predictability. *In vitro* assays cannot easily assess cell-cell interactions that may be important in a particular pathological state. Furthermore a therapeutic agent must accomplish several tasks to be effective: it must be delivered into circulation and interact at the proper site of action, and it must do so at a therapeutic concentration and remain effective for a sufficient period of time. *In vitro* assays cannot duplicate the

complex conditions of *in vivo* therapy. In assays, the agent is in contact with the cells during the entire exposure period, whereas in the case of *in vivo* therapy, exposure at the target site may be delayed or insufficient.

In view of the above, it is the Examiner's position that the specification is not commensurate in scope with the claims. And furthermore, the specification provides inadequate instruction to allow one skilled in the art to practice the claimed invention within the parameters of *in vivo* testing as implied in the method claim with a reasonable expectation of success and without undue experimentation.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 49-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation "immunogenic amino acid" in claim 49 is vague and indefinite. It is not clear which amino acids are regarded as immunogenic. The metes and bounds of the claim cannot be determined.

b. Claim 49, lines 16 and 17 is vague and indefinite in the recitation, " consists of an amino acid sequence...said group, or". The phrase seems to be redundant and similar in context to the preamble of lines 1-7 of the said claim. Applicants are requested to clarify.

c. Claim 50 is vague and indefinite in the recitation "one additional component". The additional component can be anything, a peptide, an organic molecule, an inorganic molecule, carbohydrate, etc. The claims must be so definite as to allow the comparison with the available art and for the public to determine from the claims what they encompass.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (703) 306-5880. The examiner can normally be reached on 7:00 am to 4:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne "Bonnie" Eyler, Ph.D. can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER
2/09/2004

Alana M. Harris, Ph.D.
05 February 2004